

# CONCERT GENETIC TESTING: KIDNEY DISORDERS

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Reference Number: LA.CP.CG.11

Date of Last Revision 09/23

[Coding implications](#)

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See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

## OVERVIEW

Inherited kidney disorders and inherited disorders that indirectly affect the kidneys can be more common, such as autosomal dominant polycystic kidney disease, or more rarely Lowe syndrome and Fabry disease. Identifying the genetic cause of an inherited kidney disorder can help direct treatment, inform family members, and contribute to the overall understanding of the genetic etiology of chronic kidney disease. More advanced next-generation sequencing, such as exome sequencing and comprehensive genetic testing panels, are emerging as a first-line diagnostic method for patients with chronic kidney disease.

## POLICY REFERENCE TABLE

Below is a list of higher volume tests and the associated laboratories for each coverage criteria section. This list is not all inclusive.

### Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2022, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only and may not support medical necessity. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

**NOTE: Coverage is subject to each requested code's inclusion on the corresponding LDH fee schedule. Non-covered codes are denoted (\*) and are reviewed for Medical Necessity for members under 21 years of age on a per case basis.**

<a href="#">Coverage Criteria Sections</a>	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	<a href="#">Ref</a>
<a href="#">Polycystic Kidney Disease</a>				
<a href="#">Targeted Variant Analysis</a>	Targeted Mutation Analysis for a Known Familial Variant	81403*		8
			Q61, N18	1, 2
<a href="#">Single gene or Multigene Panel</a>	Autosomal Dominant Polycystic Kidney Disease via the PKD1 Gene (PreventionGenetics)	81407*, 81479		
	PKD2 Full Gene Sequencing and Deletion/Duplication (Invitae)	81406*, 81479		
	Autosomal Recessive Polycystic Kidney Disease (ARPKD) via the PKHD1 Gene (PreventionGenetics)	81408*, 81479		
	Autosomal Dominant Polycystic Kidney Disease (ADPKD) via the GANAB Gene (PreventionGenetics)	81479		
	Autosomal Dominant Polycystic Kidney Disease (ADPKD) via the DNAJB11 Gene (PreventionGenetics)			
	Hereditary Cystic Kidney Diseases Panel (PreventionGenetics)	81404*, 81405*, 81406*, 81407*, 81408*, 81479		
	Polycystic Kidney Disease Panel (GeneDx)			
<a href="#">Comprehensive Kidney Disease Panels</a>				
<a href="#">Comprehensive Kidney Disease Panels</a>	RenaSight (Natera)	81401*, 81402*, 81403*, 81404*, 81405*, 81406*, 81407*, 81408*, 81479	N00 through N08, N10 through N16, N17 through N19, Q61, R31	3
	KidneySeq Version 5 Comprehensive Testing (Iowa Institute of Human Genetics)			
	RenalZoom (DNA Diagnostic Laboratory - Johns Hopkins Hospital)			

<u>Donor-Derived Cell Free DNA for Kidney Transplant Rejection</u>				
<u>Donor-Derived Cell Free DNA for Kidney Transplant Rejection</u>	Allosure Kidney (CareDx, Inc.)	81479	T86.11, T86.12, Z94.0	7
	Prospera Kidney (Natera)			
	Viracor TRAC Kidney dd-cfDNA (Viracor Eurofins)	0118U*		
<u>Other Covered Kidney Disorders</u>				
<u>Other Covered Kidney Disorders</u>	See list below	81400* through 81408*, 0268U*		4, 5, 6

## OTHER RELATED POLICIES

This policy document provides coverage criteria for hereditary kidney disorders. Please refer to:

- *Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay* for coverage criteria related to genetic disorders that affect multiple organ systems
- *Genetic Testing: Hereditary Cancer Susceptibility* LA.CP.MP 225c for coverage criteria related to von Hippel Lindau (VHL) syndrome and other hereditary cancer syndromes.
- *Genetic Testing: General Approach to Genetic Testing* for coverage criteria related to genetic testing for kidney disease that is not specifically discussed in this or another non-general policy.

## CRITERIA

It is the policy of Louisiana Healthcare Connections that the specific genetic testing noted below is **medically necessary** when meeting the related criteria:

## POLYCYSTIC KIDNEY DISEASE

### Targeted Variant Analysis

- I. *PKD1*, *PKD2*, *GANAB*, or *DNAJB11* targeted variant analysis (81403\*) to establish a diagnosis of autosomal dominant polycystic kidney disease is considered **medically necessary** when:

- A. The member/enrollee has a close relative with a known pathogenic or likely pathogenic variant in *PKD1*, *PKD2*, *GANAB*, or *DNAJB11*.
- II. *PKHD1* targeted variant analysis (81403\*) to establish a diagnosis of autosomal recessive polycystic kidney disease is considered **medically necessary** when:
  - A. The member/enrollee has a sibling with known biallelic pathogenic or likely pathogenic variants in *PKHD1*.
- III. *PKD1*, *PKD2*, *GANAB*, *DNAJB11*, or *PKHD1* targeted variant analysis (81403\*) to establish a diagnosis of autosomal dominant or autosomal recessive polycystic kidney disease is considered **investigational** for all other indications.

### Single Gene or Multigene Panel

- I. *PKD1* (81407\*, 81479), *PKD2* (81406\*, 81479), *GANAB* (81479), *DNAJB11* (81479), *PKHD1* (81408\*, 81479) sequencing and/or deletion/duplication analysis or multigene panel analysis (81404\*, 81405\*, 81406\*, 81407\*, 81408\*, 81479) to confirm or establish a diagnosis of polycystic kidney disease is considered **medically necessary** when:
  - A. The member/enrollee has any of the following clinical features of polycystic kidney disease:
    1. Multiple bilateral renal cysts, **OR**
    2. Cysts in organs other than the kidneys (especially the liver, seminal vesicles, pancreas, and arachnoid membrane), **OR**
    3. Hypertension in an individual younger than age 35, **OR**
    4. Intracranial aneurysm, **OR**
    5. Bilaterally enlarged and diffusely echogenic kidneys, **OR**
    6. Poor corticomedullary differentiation, **OR**
    7. Hepatobiliary abnormalities with progressive portal hypertension, **OR**
    8. Congenital hepatic fibrosis (CHF) with portal hypertension.
- II. *PKD1* (81407\*, 81479), *PKD2* (81406\*, 81479), *GANAB* (81479), *DNAJB11* (81479), *PKHD1* (81408\*, 81479) sequencing and/or deletion/duplication analysis or multigene panel analysis (81404\*, 81405\*, 81406\*, 81407\*, 81408\*, 81479) to confirm or establish a diagnosis of polycystic kidney disease is considered **investigational** for all other indications.

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## COMPREHENSIVE KIDNEY DISEASE PANELS

- I. Genetic testing for kidney disease via a comprehensive kidney disease panel (81401\*, 81402\*, 81403\*, 81404\*, 81405\*, 81406\*, 81407\*, 81408\*, 81479) is considered **medically necessary** when:
  - A. The member/enrollee has chronic kidney disease with an undetermined cause after undergoing standard-of-care workup studies (examples: history and physical examination, biochemical testing, renal imaging, or renal biopsy), **AND**
  - B. The member/enrollee meets at least one of the following:
    1. Onset of chronic kidney disease under 40 years of age, **OR**
    2. One or more [first- or second-degree relatives](#) with chronic kidney disease, **OR**
    3. Consanguineous family history, **OR**
    4. Cystic renal disease, **OR**
    5. Congenital nephropathy.
- II. Genetic testing for kidney disease via a comprehensive kidney disease panel (81401\*, 81402\*, 81403\*, 81404\*, 81405\*, 81406\*, 81407\*, 81408\*, 81479) is considered **investigational** for all other indications.

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## DONOR-DERIVED CELL-FREE DNA FOR KIDNEY TRANSPLANT REJECTION

- I. The use of peripheral blood measurement of donor-derived cell-free DNA in the management of patients after renal transplantation (81479, 0118U\*) is considered **investigational** for all indications, including but not limited to:
  - A. Detection of acute renal transplant rejection
  - B. Detection of renal transplant graft dysfunction

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## OTHER COVERED KIDNEY DISORDERS

The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis.

- I. Genetic testing to establish or confirm one of the following genetic kidney disorders to guide management is considered **medically necessary** when the member/enrollee demonstrates clinical features\* consistent with the disorder (the list is not meant to be comprehensive, see II below):
  - A. [Alport Syndrome](#)
  - B. [C3 Glomerulopathy](#)
  - C. Congenital nephrotic syndrome
  - D. [Cystinosis](#)
  - E. Cystinuria
  - F. [Fabry Disease](#)
  - G. [Genetic \(familial\) atypical hemolytic-uremic syndrome \(aHUS\)](#)
  - H. Primary Hyperoxaluria
- II. Genetic testing to establish or confirm the diagnosis of all other kidney disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic Testing* (see policy for coverage criteria).

\*Clinical features for a specific disorder may be outlined in resources such as [GeneReviews](#), [OMIM](#), [National Library of Medicine](#), [Genetics Home Reference](#), or other scholarly source.

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## NOTES AND DEFINITIONS

1. Close relatives include first, second, and third degree blood relatives on the same side of the family:
  - a. **First-degree relatives** are parents, siblings, and children
  - b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
  - c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

# BACKGROUND AND RATIONALE

## Polycystic Kidney Disease - Targeted Variant Analysis

### *Genetic Support Foundation*

The Genetic Support Foundation's Genetics 101 information on inheritance patterns says the following about testing for familial pathogenic variants:

Genetic testing for someone who may be at risk for an inherited disease is always easier if we know the specific genetic cause. Oftentimes, the best way to find the genetic cause is to start by testing someone in the family who is known or strongly suspected to have the disease. If their testing is positive, then we can say that we have found the familial pathogenic (harmful) variant. We can use this as a marker to test other members/enrollees of the family to see who is also at risk.

## Polycystic Kidney Disease - Single Gene or Multigene Panel

*GeneReviews: Polycystic Kidney Disease, Autosomal Dominant and Polycystic Kidney Disease, Autosomal Recessive*

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online. The recommended polycystic kidney disease testing for autosomal dominant polycystic kidney disease (ADPKD) and autosomal recessive polycystic kidney disease (ARPKD) is as follows:

“ADPKD should be suspected in individuals with the following:

- Multiple bilateral renal cysts and the absence of manifestations suggestive of a different renal cystic disease
- Cysts in other organs, especially the liver, but also seminal vesicles, pancreas, and arachnoid membrane...
- Hypertension in an individual younger than age 35 years
- An intracranial aneurysm...”

“Autosomal recessive polycystic kidney disease (ARPKD) should be suspected in individuals with bilaterally enlarged, diffusely echogenic kidneys...[and] one or more of the following:...Clinical/laboratory signs of congenital hepatic fibrosis (CHF) that leads to portal hypertension...”

“The renal diagnostic criteria for ARPKD detected by ultrasonography are:

- Increased renal size (in relation to normative size based on age and size of the affected individual);
- Increased echogenicity;

- Poor corticomedullary differentiation”

“[In] Childhood and young adulthood...The hepatobiliary abnormalities with progressive portal hypertension are often the prominent presenting features.”

## Comprehensive Kidney Disease Panels

*Hays et al (2020)*

“We propose the following approach, based on a review of current literature and our practical experience. This approach assumes individuals have already undergone an initial nephrologic workup, including biochemical and serologic testing, imaging of the kidneys, and renal biopsy if indicated.

...[A]fter a negative or inconclusive initial workup, a patient is considered to have KDUE [kidney disease of unknown etiology] and may then be stratified according to the probability of a genetic disease. We consider higher probability patients as those with the following risk factors: early-onset disease (age <40 years), a positive family history of CKD [chronic kidney disease], consanguinity, extrarenal anomalies, cystic renal disease, or congenital nephropathy”. (p. 594)

## Donor-Derived Cell-Free DNA for Kidney Transplant Rejection

*Knight et al (2019)*

A publication in the journal Transplantation entitled “Donor-specific Cell-free DNA as a Biomarker in Solid Organ Transplantation. A Systematic Review” stated the following:

In summary, donor-derived cfDNA shows promise as a biomarker for the detection of acute transplant graft injury. It has potential to reduce the need for protocol biopsy surveillance, allowing for a more targeted diagnostic approach. Detection of injury occurs before clinical manifestation, meaning that there is a window for earlier detection and treatment of AR [acute rejection] and other causes of graft injury with the potential to improve outcomes. It may also facilitate the detection of under immunosuppression and find use as a tool for monitoring during immunosuppression minimization. Further studies are required to validate the thresholds for further investigation and intervention, determine the optimum frequency for monitoring, and to identify whether prospective monitoring using dd-cfDNA can indeed improve transplant outcomes compared to current practice. (p. 280)

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Reviews, Revisions, and Approvals	Revision Date	Approval Date
Converted corporate to local policy.	09/23	11/27/23



## REFERENCES

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### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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